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## Safe motherhood : severe maternal morbidity in the Netherlands. The LEMMoN study

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# CHAPTER 7

## Eclampsia in the Netherlands

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## **Abstract**

**Objective:** The incidence of maternal mortality due to hypertensive disorders of pregnancy in the Netherlands is greater than in other Western countries. We aimed to confirm and explain this difference by assessing incidence, risk factors, and substandard care of eclampsia in the Netherlands.

**Methods:** In a nationwide population-based cohort study, all cases of eclampsia were prospectively collected during a 2-year period (2004 –2006). All pregnant women in the Netherlands in the same period acted as reference cohort (n=371,021). Substandard care was assessed in all cases. A selection of cases was extensively audited by an expert panel. Main outcome measures were incidence, case fatality rate, possible risk factors, and substandard care.

**Results:** All 98 Dutch maternity units participated (100%). There were 222 cases of eclampsia, for an incidence of 6.2 per 10,000 deliveries. Three maternal deaths occurred; the case fatality rate was 1 in 74. Risk factors in univariable analysis included multiple pregnancy, primiparity, young age, ethnicity, and overweight. Prophylactic magnesium sulphate was given in 10.4% of women, and antihypertensive medication was given in 39.6% of women with a blood pressure on admission at or above 170/110 mm Hg. Additionally, substandard care was judged to be present by an expert panel in 15 of 18 audited cases (83%).

**Conclusion:** The incidence of eclampsia in the Netherlands is markedly increased as compared with other Western European countries. Substandard care was identified in many cases, indicating the need for critical evaluation of the management of hypertensive disease in the Netherlands.

## **Introduction**

Hypertensive disorders of pregnancy are one of the leading causes of maternal mortality and severe maternal morbidity worldwide. In the Netherlands, eclampsia/preeclampsia is the leading cause of maternal mortality, accounting for 60% of direct maternal deaths (Schutte JM, Steegers EA, Schuitemaker NW, Santema JG, de Boer K, Pel M, et al. Rise in maternal mortality in the Netherlands 1993–2005 [in press]).<sup>1</sup> The incidence of eclampsia has decreased dramatically over the past century in Western countries due to improved antenatal care and early management. Over the past decades, the incidence seemed to have stabilized, but since the publication of the Collaborative Eclampsia trial (1995)<sup>2</sup> and the Magpie trial (2002)<sup>3</sup>, advocating the therapeutic and prophylactic use of magnesium sulphate, a further decline of incidence has been achieved in some countries.<sup>4–6</sup> Reported national incidences in Western European countries range from 2.4 per 10,000 deliveries in Finland to 5.7 per 10,000 deliveries in Sweden.<sup>7,8</sup>

Patient safety and adherence to national guidelines are key issues in the reduction of maternal and neonatal morbidity and mortality. In the presence of ample evidence for minimal standards provided by randomized trials, there is an unquestionable need for uniform application of standard approaches provided by guidelines. It is the aim of the Dutch Society of Obstetrics and Gynaecology to contribute to the development of evidence-based standardized approaches.

The primary aim of this study was to assess whether the incidence of eclampsia in the Netherlands is increased as compared with other European countries, as is the case for maternal death due to hypertensive disorders.<sup>9</sup> Secondly, we aimed to assess the management of eclampsia to explain the differences.

## **Materials and Methods**

This study is part of a broader, nationwide enquiry into severe maternal morbidity in the Netherlands, called Nationwide Study Into Ethnic Determinants of Maternal Morbidity in the Netherlands (LEMMoN).<sup>10</sup> In this study, which enrolled cases from August 1, 2004, until August 1, 2006, all Dutch obstetric units participated. In the Netherlands, there are 10 tertiary care hospitals, 33 non-academic teaching hospitals, and 55 general hospitals with an obstetric ward. In 2005, the number of deliveries per hospital ranged from 93 to 2,655. Women with high-risk pregnancies and those with low-risk pregnancies who develop complications during pregnancy or child birth deliver in the hospital under the guidance of obstetricians (secondary or tertiary care, 59% of all births). Women with low-risk pregnancies without complications deliver under the guidance of midwives or family physicians (primary care), either at home (30% of all births) or in hospital under their responsibility (11% of all births). Most women with onset of preeclampsia before 32 weeks of gestational age are referred to a tertiary care centre. Any case

of eclampsia occurring outside of a hospital will be referred to a hospital and thus be notified. Eclampsia was defined as the occurrence of convulsions superimposed on preeclampsia and not attributable to other causes. Requests for notification of cases of eclampsia, along with other types of severe maternal morbidity, were sent to all local coordinators on a monthly basis. Cases were communicated to the National Surveillance Centre for Obstetrics and Gynaecology in a Web-based design by mentioning date of birth and initials of the woman. If no cases of eclampsia occurred, this was also reported. Reminders were sent to nonresponders every month until they had returned the monthly notification card. Local sources used by the local coordinators included daily staff meetings, labour ward delivery registers, intensive care admission registers, discharge registers, and personal communication.

After notification, a case record form was sent to us, accompanied by photocopies (made anonymous) of all relevant parts of the hospital case notes and correspondence. A detailed review of cases was completed by one of the researchers (J.J.Z.), and all cases were entered into an Access (Microsoft Corp., Redmond, WA) database. If information was deemed insufficient, additional data were requested. Cases of maternal mortality were reported to the national Maternal Mortality Committee of the Dutch Society for Obstetrics and Gynaecology by the attending obstetrician as usual. These cases were eventually added to the database.

We recorded maternal characteristics (age, body mass index, parity, and ethnicity), all variables concerning pregnancy and delivery, and neonatal outcome. We also recorded data on the specific complication, like seizure-to-delivery interval, number of seizures, symptoms and signs, blood pressures, laboratory values, and medicaments administered. A total of 130 items were entered into the database for each case. Characteristics of each hospital were also recorded (university or teaching hospital and annual number of deliveries).

Ethnicity was defined by country of origin ("geographical ethnic origin") and categorized according to the most common population groups in the Netherlands (Western, Moroccan, Surinam, Dutch Caribbean, Turkish, sub-Saharan African, Middle East, and Far East). We used the definitions of Statistics Netherlands, based on country of birth of the woman. Substandard care was defined as malcompliance with the recommendations in the guideline "Hypertensive Disorders in Pregnancy" of the Dutch Society of Obstetrics and Gynaecology<sup>11</sup> and was assessed in two different ways: first, substandard treatment of hypertension and prophylaxis of seizures according to the national guideline was assessed in all cases by the first author. Second, substandard care as judged by a national panel of experts analogously to the methodology of the ongoing analysis of maternal mortality in the Netherlands was assessed in a subgroup of 18 women. For this purpose, an audit meeting was organized. The panel, consisting of members of the Maternal Mortality Committee, members of the LEMMoN expert panel, members of the Managing Obstetric Emergencies and

Trauma course, and local staff of the 12 hospitals involved, assessed 12 cases of complicated eclampsia, selected by purposive sampling (cases with ICU admission, multiple seizures and availability of sufficient data). Substandard care was assessed using a standardized form with items related to patient, care providers and health care system, based on the national guideline.<sup>11</sup> A further six cases of eclampsia, which were assessed likewise during general audit meetings of the LEMMoN study, were added before analysis.

Main outcome measures of the study were incidence, case fatality rate, possible risk factors, and substandard care. Denominator data for the number of births in the Netherlands during the exact study period were obtained from Statistics Netherlands.<sup>12</sup> Births are registered based on birth certificates, which are required by law beyond 24 weeks of gestational age in the Netherlands. Reference values for possible risk factors for eclampsia were obtained from Statistics Netherlands (exact study period) and The Netherlands Perinatal Registry (LVR-2; 2005).<sup>13</sup> The Netherlands Perinatal Registry is the Dutch national perinatal database which covers nearly 100% of births under guidance of the obstetrician, in which parity, gestational age at delivery, mode of delivery, and place of antenatal care (midwife or obstetrician) are reliably registered. Each case is entered into the database by the attending clinician directly after birth. Data that were compared between cases and noncases was collected using the same fact-sheet from LVR-2.

Case fatality rate was calculated by dividing the number of deaths by the total number of cases. To control for underreporting, we cross-matched our database with the Dutch perinatal database (LVR-2).<sup>13</sup> During a 5-month period, cases of eclampsia reported to this database but not to us were identified and local coordinators were asked to reanalyze these cases and report when appropriate. Relative risks and confidence intervals were calculated in univariable analysis. Differences between groups were identified using  $\chi^2$ , and significance was defined as  $P < .05$ . Statistical analysis was performed using Statistical Package for the Social Sciences 14.0 (SPSS Inc., Chicago, IL). The study was centrally reviewed by the institutional review board of Leiden University Medical Centre, and approval was obtained.

## Results

All 98 obstetric units in the Netherlands participated in the study. During the study period, there were 371,021 deliveries in the Netherlands. From all 2,352 (98 hospitals, 24 months) monthly notification cards, 97% were returned, representing 358,874 deliveries.

Four of 226 reported cases of eclampsia were excluded because seizures were obviously caused by another illness, leaving 222 cases of eclampsia. For nine reported cases, we received no detailed data after notification, leaving a total of 213 cases available for analysis. Characteristics of women are shown in Table 1.

**Table 1. Characteristics of study population.**

	<i>Eclampsia</i>		<i>No eclampsia</i>	
	<i>n</i>	(%)	<i>n</i>	(%)
Age (mean 30.0 vs. 31.1)				
< 20 year	8	(3.8)	4645	(1.2)
20-35 year	160	(75.1)	279,026	(74.1)
35-40 year	39	(18.3)	79,756	(21.2)
≥ 40 year	6	(2.8)	13,056	(3.5)
Parity				
0	149	(70.0%)	169,971	(45.1%)
>0	64	(30.0%)	206,512	(54.9%)
Body Mass Index (BMI; kg/m <sup>2</sup> )				
<18.5	5	(3.5)	n/a	(3.1)
18.5 - 24.9	84	(59.2)	n/a	(65.2)
25.0-29.9 (overweight)	33	(23.2)	n/a	(22.6)
≥ 30.0 (obese)	20	(14.1)	n/a	(9.1)
unknown	71			
Geographical ethnic origin				
Netherlands	147	(69.3)	280,752	(74.5)
Morocco/Turkey	16	(7.6)	29,368	(7.8)
Surinam/Dutch Antilles	15	(7.1)	13,211	(3.5)
other non-Western	25	(14.6)	20,552	(5.5)
other Western	9	(1.4)	32,812	(8.7)
unknown	1			

**n/a: not available.**

The incidence of eclampsia was 6.2 per 10,000 deliveries. There were three maternal deaths due to eclampsia, giving a case fatality rate of 1.4% (1 in 74). One woman died at home after repeated refusal of admission, two others died in the hospital after spontaneous term delivery. Other severe maternal and neonatal complications are listed in Table 2. Incidence varied largely by hospital, ranging from 0 to 30.9 per 10,000. The mean “hospital incidence” (only concerning cases under responsibility of the obstetrician) was 9.0 per 10,000 overall, 18.1 for tertiary care centres, and 8.5 for general hospitals. Incidence figures did not differ by volume of maternity unit (data not shown). First seizure occurred antepartum in 39.4%, intrapartum in 32.4%, and postpartum in 28.2% of cases. The median interval between first seizure and delivery was 8 hours for antepartum eclampsia (range 20 minutes to 11 days) and 1 hour for intrapartum eclampsia (range 0 minutes to 7 hours). For postpartum eclampsia, the median delivery-to-seizure interval was 5 hours (range 1 minute to 8 days). Fifty-one women (24.1%) had multiple seizures (range 2–5). The average duration of gestation was 37 weeks (range 22–42). Forty-one percent of the cases occurred preterm, 58% occurred at term (37–42 weeks of gestation), and 1% post term. Preterm eclampsia occurred more often antepartum (odds ratio 9.9; 95% confidence interval 5.2–18.8), whereas at term eclampsia occurred more often intrapartum or postpartum.

**Table 2. Major maternal and fetal complications**

Complication*	number*	% of cases
<i>Maternal</i>		
Maternal death	3	1.4
ICU admission	89 (2)	41.8
HELLP	49 (1)	23.0
Referral to tertiary care centre	30	14.1
Major obstetric haemorrhage ( $\geq 10$ pc)	7	3.3
Cerebrovascular accident	7 (1)	3.3
Coma	5 (1)	2.3
(Suspicion of) placental abruption	5	2.3
Transient blindness	4	1.9
ARDS	3 (1)	1.4
Reversible Posterior Leuco-encephalopathy Syndrome	3	1.4
Pulmonary embolism	3	1.4
Two cases each of the following: disseminated intravascular coagulation (1), renal dialysis, sepsis, pneumonia	2	0.9
One case each of the following: cerebral oedema (1), hydrocephalus, Budd-Chiari syndrome, iatrogenic perforation of the stomach, conus-cauda syndrome due to intraspinal bleeding, myocardial ischemia, liver hematoma	1	0.5
<i>Fetal (data available for 132 neonates)</i>		
Intra uterine death	7 (1)	5.3
Neonatal death	4	3.0
pH < 7.00	10	9.1

\* **between brackets are numbers occurring in cases of maternal death**

Multiple pregnancy, primiparity, young age, ethnicity, overweight, and complete antenatal care by the obstetrician were the most important factors associated with eclampsia (Table 3). In 18 women (8.5%) obstetric history revealed pregnancy-induced hypertension, preeclampsia or haemolysis, elevated liver enzymes, and low platelets syndrome. Thirteen women (6.1%) had pre-existent hypertension, six of whom were on antihypertensive medication before pregnancy.

Twenty percent of women had their first antenatal visit beyond 14 weeks of gestation, 7% beyond 20 weeks, and three women only booked at 32, 33, and 35 weeks of gestation. Two women had had no antenatal care at all at the moment of eclampsia. Booking was at least 1 month before the first seizure in all but four women.

In 38 cases (18%), the first seizure occurred at home, in six of them during or shortly after home delivery and in three others after discharge after hospital delivery. Twenty of these women had more than one seizure (54% of all out of hospital eclampsia cases). Of all 175 women experiencing eclampsia in the hospital, 111 (63.4%) were diagnosed as having preeclampsia on admission, and another 20 (11.4%) were admitted because of pregnancy-induced hypertension. Forty-four women (25.1%) were not known to be hypertensive and were admitted for other reasons, all but two intrapartum. The two women, who experienced antepartum eclampsia in the hospital, were admitted for regulation of diabetes and for observation of antepartum haemorrhage.

The mean systolic and diastolic blood pressure readings on admission were 157 mm Hg (range 105–230) and 98 mm Hg (range 57–137) among the 175 women with eclampsia in hospital and 169 mm Hg (range 80–240) and 109 mm Hg (range 60–164) among the women with eclampsia at home. On admission, 47.4% of cases had severe preeclampsia according to the criteria of the Dutch guideline.<sup>11</sup> Although prophylaxis of seizures is advised in these cases, only 15.4% received magnesium sulphate (Table 4). Premonitory signs and symptoms included headache (69%), upper abdominal pain (45%), nausea (49%), vomiting (28%), visual disturbances (41%), and hyperreflexia (55%). In 23 cases (10.8%), eclampsia occurred without any of these signs.

**Table 3. Possible risk factors for eclampsia**

<i>risk factor</i>	<i>Eclampsia</i>	<i>No eclampsia</i>	<i>RR (95% C.I.)</i>
Patient			
age < 20	3.8%	1.2% <sup>†</sup>	3.1 (1.5-6.3)
age < 25	17.8%	11.5% <sup>†</sup>	1.7 (1.2-2.4)
age ≥ 35	21.1%	24.7% <sup>†</sup>	0.8 (0.6-1.1)
BMI ≥ 25 (overweight)	37.3%	31.7% <sup>†</sup>	1.3 (0.9-1.8)
BMI ≥ 30 (obese)	14.1%	9.1% <sup>†</sup>	1.6 (1.0-2.6)
non-Western immigrant	26.4%	16.8% <sup>†</sup>	1.8 (1.3-2.4)
Surinam/Dutch Caribbean immigrant	9.6%	4.0% <sup>†</sup>	2.5 (1.3-4.9)
sub-Saharan African immigrant	6.8%	1.3% <sup>†</sup>	6.2 (3.6-10.6)
Pregnancy			
initial antenatal care by obstetrician	29.7%	14.3% <sup>‡</sup>	2.5 (1.9-3.4)
parity 0	70.0%	45.2% <sup>†</sup>	2.8 (2.1-3.8)
parity ≥ 3	2.4%	5.0% <sup>†</sup>	0.5 (0.2-1.1)
multiple pregnancy	9.9%	1.7% <sup>†</sup>	6.2 (4.0-9.7)
artificial reproduction techniques: IVF/ICSI	3.8%	1.9% <sup>14</sup>	2.0 (1.0-4.0)
Delivery (only for postpartum eclampsia, n=60)			
home delivery	8.3%	31.6% <sup>†</sup>	0.2 (0.1-0.5)
induction of labour	41.7%	12.5% <sup>‡</sup>	5.0 (3.0-8.4)
caesarean delivery without labour	18.7%	5.9% <sup>‡</sup>	3.7 (1.9-7.0)
ventouse/forceps	13.3%	8.6% <sup>‡</sup>	1.6 (0.8-3.4)
caesarean delivery overall	26.7%	14.0%	2.2 (1.3-4.0)
preterm birth (<37w)	31.7%	5.8% <sup>‡</sup>	7.5 (4.4-13.0)
post term birth (≥42w)	3.3%	4.3% <sup>‡</sup>	0.8 (0.2-3.1)

National reference values from <sup>†</sup>CBS (exact study period) and <sup>‡</sup>LVR-2 (2005).

In 9.9% of all cases, eclampsia occurred despite prophylactic administration of magnesium sulphate. Magnesium sulphate was eventually administered in 96.2%. In 50.5% of these women diazepam was administered first. In the remaining cases, only diazepam was administered (n=3), treatment was only started after emergency caesarean delivery because of eclampsia (n=1),

treatment consisted of valproic acid (n=1), or maternal death occurred at home (n=1). Among the 51 women with multiple seizures, magnesium sulphate was initiated before the first seizure in four cases (7.8%), after the first seizure in 14 cases (31.1%), and only after the second or third seizure in 23 (51.1%) and four cases (8.9%), respectively. Three of the latter four concerned eclampsia at home, and successive seizures occurred in the ambulance or upon arrival at the hospital.

Antihypertensive treatment was initiated before the first seizure in 44 of 175 women (26.3%) with eclampsia in the hospital. On admission, 49 women (35.2%) had a systolic or diastolic blood pressure at or above the threshold of 170/110 mm Hg.<sup>11</sup> In only 20 (40.8%) of these, antihypertensive drugs were initiated at that moment (Table 5). The most used intravenous agents were ketanserin (55.4%), labetalol (33.3%), and dihydralazine (8.3%).

**Table 4. Warning signs and symptoms on admission in women and MgSO<sub>4</sub> prophylaxis**

Trigger	Specification	overall (n=175)	on MgSO <sub>4</sub> [n=22 (12.6%)]	% of women with the feature*
Symptoms	severe headache/abdominal tenderness/ visual disturbances	61	14 (23.0%)	41.5%
Signs	severe hyperreflexia	23	8 (34.8%)	23.2%
lab values	liver enzymes >45; creatinin >100; thrombocytes <100	66	8 (12.1%)	51.2%
Proteinuria	stick + or >= 0.3 g/24h	102	13 (12.7%)	82.9%
Hypertension	diastolic BP >=110 or systolic BP >=170	49	10 (20.4%)	35.3%
severe PE <sup>†</sup>	BP >= 170/110 or BP >= 160/100 with serious symptoms/signs	65	10 (15.4%)	47.4%

BP, blood pressure; \*cases where presence of the item is unknown were excluded; <sup>†</sup>according to the Dutch Guideline Hypertensive disease in pregnancy.

After cross-matching with the Dutch Perinatal Database, nine cases seemed not to have been reported to us. After a request for reanalysis of these cases to the local coordinators, six seemed to be incorrectly reported to the LVR as eclampsia. In one case, nobody responded to our request for reanalysis, and only two cases (3%) seemed to be truly underreported. These two cases were as yet reported. Because the underreporting seemed to be low, we decided not to repeat this analysis for the remainder of the study period.

During the plenary audit meetings, substandard care was judged to be present in 15 of 18 cases (83%; 95% confidence interval 59–96%) by the majority of assessors. In more than one half of these cases, substandard care was further classified as “major,” indicating that different management might well have resulted in a different outcome. The majority of substandard care (87% of 312 items scored in total) was found at the level of the care providers, the main items being inadequate treatment of hypertension and inadequate seizure prophylaxis (33% and 38% of 225 eclampsia-related items scored, respectively).

**Table 5. Blood pressure and antihypertensive treatment for eclampsia in the hospital (n=175)**

Threshold	n	% of total*	antihypertensive treatment n(%)		
			i.v.	Oral	none
BP on admission: diast>=110 or syst>=170	49	35.2	12 (24.5)	8 (16.3)	29 (59.2)
BP on admission: diast>=110	28	18.8	9 (32.1)	6 (21.4)	13 (46.4)
BP on admission: syst>=170	38	27.3	11 (28.9)	5 (13.2)	22 (57.9)
Severe pre-eclampsia on admission†	65	47.4	17 (25.8)	12 (18.2)	36 (54.5)
Highest recorded BP: diast>=110 or syst>=170	135	86.5	22 (16.3)	22 (16.3)	91 (67.4)

BP, blood pressure; \*cases where blood pressure on admission is unknown were excluded; †according to the Dutch guideline 'Hypertensive Disease in Pregnancy'<sup>11</sup> (BP >= 170/110 or BP >= 160/100 with serious symptoms/signs)

## Discussion

The incidence of 6.2 per 10,000 is clearly increased as compared with other neighbouring European countries (Table 6).

**Table 6. Population-based incidence of eclampsia**

Country	Period	n	Incidence (/10,000)
<i>Europe</i>			
Sweden <sup>16</sup>	1976-1980	74	2.9
Iceland <sup>15</sup>	1972-1991	40	4.6
Sweden <sup>17</sup>	1991-1992	80	3.3
UK <sup>18</sup>	1992	383	4.9
Finland <sup>7</sup>	1990-1994	77	2.4
Scandinavia <sup>8</sup>	1998-2000	210	5.0
Scotland <sup>22</sup>	2001-2002	25	4.9
Scotland <sup>4</sup>	2003-2005	55	3.5
UK <sup>5</sup>	2005-2006	214	2.7
<b>Netherlands</b>	<b>2004-2006</b>	<b>222</b>	<b>6.2</b>
<i>Other</i>			
USA <sup>20</sup>	1979-1986		5.6
USA* <sup>21</sup>	1988-1997	300	10.0
Canada <sup>19</sup>	1991-2001	973	3.8

\* representative sample instead of nationwide cohort

Especially when compared with the more recently published studies in the United Kingdom and Scotland, our incidence seems to be twice as high. The results of our study are in line with earlier findings: maternal mortality due to hypertensive disorders in the Netherlands is three times as high as in the UK<sup>6</sup>, and recent analysis revealed that substandard care was present in 26 of 27 cases.<sup>1</sup> Substandard treatment of hypertension was found in at least 60% of women and magnesium sulphate for seizure prophylaxis was administered in only 10% of cases, although we classified 47%

of cases as severe preeclampsia already on admission. The results of a clinical audit of a subset of 18 cases confirmed these findings. The nationwide design and support of this study, with 100% participation of Dutch maternity units, is its major strength. The major limitation of this study is that we did not collect individual data for the reference cohort of pregnant women in the Netherlands. Instead, we used nationwide incidence figures, which made it impossible to adjust relative risks for confounding variables in a multivariable model. Furthermore, despite multiple efforts, we cannot be sure that all cases have been reported to us. However, a cross-check for underreporting through the national perinatal database revealed minimal underreporting. Finally, we would have liked to have more cases assessed by the audit committee already, but unfortunately time and resources were limited. Substandard antihypertensive treatment and seizure prophylaxis, however, were assessed in all cases by the first author, and the audit process is continuing.

Our first concern is to check whether the reported cross-country difference is true or artificial, i.e., confounded by differences in study design or inclusion criteria. The Scottish ongoing surveillance system for eclampsia and other severe morbidities is very similar to our system and seems very reliable.<sup>6,22</sup> The two nationwide studies from the United Kingdom in 1992 and 2005 were both thoroughly expedited and had a very similar study design as ours.<sup>5,18</sup> Only the definition of eclampsia was stricter in the United Kingdom studies, thereby excluding 31 cases reported as eclampsia because abnormal laboratory values could not be confirmed. We doubt whether these cases should have been excluded, because eclampsia is primarily a clinical diagnosis, and abnormal laboratory values are not obligatory in our opinion. The incidence in the most recent study of Knight et al<sup>5</sup> would be only slightly higher (3.1/10,000) when cases were not excluded based on their definitions. Thus, our incidence of eclampsia seems to be truly increased. Although cross-country differences in population and prevalence of preeclampsia cannot be completely ruled out, it is unlikely that these differences play a significant role in explaining the difference.

Ethnic groups showing the highest incidence in our study are even more often represented in the United Kingdom, and overweight is also more prevalent.<sup>6,23</sup> Data on cross-country differences in prevalence of preeclampsia are not available. According to the Dutch guideline, treatment of hypertension is “strongly advised” with diastolic pressure of 110 mm Hg or more or systolic pressure of 170 mm Hg or more.<sup>11</sup> It is explicitly stated in the guideline that lower thresholds should apply in case of preeclampsia with signs and symptoms. In our study, many women were not treated according to this protocol when considering the highest systolic and diastolic blood pressures. Especially, systolic blood pressure too often did not trigger start of treatment, although it has been recognized that it is associated with the most serious maternal morbidity, especially cerebrovascular accidents.<sup>24</sup> Magnesium sulphate should not be regarded as an antihypertensive agent. Also regarding the decision to deliver preeclamptic women, Dutch obstetricians tend to be

too expectant. The median gestational age of all cases at the time of first seizure or delivery in our study was 38 weeks, with eclampsia even occurring post term in three cases. This is 3 weeks more than in the United Kingdom, where delivery after stabilization is explicitly recommended after 34 weeks.<sup>5,25</sup> With 50% of all women already being hospitalized because of preeclampsia, opportunities to prevent women from experiencing eclampsia were likely missed. Delivery should be pursued after 34 weeks in case of severe preeclampsia. A final aspect that could play a role in the increased incidence of eclampsia is the fact that proteinuria is not checked routinely during antenatal visits, causing delay in detection of preeclampsia. Also, pregnant women are often not informed about warning signs, which has led to significant patient delay in some instances. Routine checking of proteinuria in women with hypertension and a patient awareness leaflet could reduce these types of delay. Because there is clear evidence that magnesium sulphate is the first-choice drug for treatment and prophylaxis of seizures, the use of diazepam should be strongly discouraged.<sup>2</sup> Incidence of hypertensive disorders in our study varied between women with different ethnic backgrounds, especially sub-Saharan African women seeming to have an increased risk (relative risk 6.2; 95% confidence interval 3.6 – 10.6). This is in agreement with other reports.<sup>6,22,26</sup> The results are also consistent with the overall increased risk to immigrant women of experiencing severe maternal morbidity in the Netherlands, but risks are more distinct for eclampsia than for other types of morbidity.<sup>10</sup> Despite several recent publications reporting declining incidences of eclampsia since the general introduction of magnesium sulphate for treatment and prophylaxis of seizures, we report a substantially higher incidence in the Netherlands as compared with other Western European countries.<sup>4,5</sup> Stricter adherence to the national guidelines is necessary to prevent eclampsia and other dramatic complications, including maternal death. The openness with which all participating obstetricians provided their data and participated in audits is encouraging, because these are important requirements for improvement in quality of care. The notion that training in obstetric emergency situations is important has become universal in the Netherlands, and the Managing Obstetric Emergencies and Trauma course is becoming an integral part of training of obstetricians and registrars. Ongoing local audit of cases of eclampsia will be implemented in the national quality assurance program to improve management and guidelines. Our study gives ample evidence that there is considerable room for improvement. Although we realize that there will always be unpreventable eclampsia, we feel that there is no reason for the Dutch incidence of eclampsia to be higher than in other Western European countries.

## References

- 1 Schutte JM, Schuitemaker NW, van Roosmalen J, Steegers EA. Substandard care in maternal mortality due to hypertensive disease in pregnancy in The Netherlands. *BJOG* 2008;115:732–6.
- 2 Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial [published erratum appears in *Lancet* 1995;346:258]. *Lancet* 1995;345:1455–63.
- 3 Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. *Lancet* 2002;359:1877–90.
- 4 Penney G, Adamson L. Scottish confidential audit of severe maternal morbidity, 4th annual report 2006. Available at: [www.nhshealthquality.org/nhsqis/files/Maternityservices\\_SP CERH30\\_4thAnnualReport\\_2006.pdf](http://www.nhshealthquality.org/nhsqis/files/Maternityservices_SP CERH30_4thAnnualReport_2006.pdf). Retrieved May 5, 2008.
- 5 Knight M, UKOSS. Eclampsia in the United Kingdom 2005. *BJOG* 2007;114:1072–8.
- 6 Lewis G, editor. Saving mother's lives: reviewing maternal deaths to make motherhood safer (2003–2005). The Seventh Report on Confidential Enquiries into Maternity Deaths in the United Kingdom. London (UK): CEMACH; 2007.
- 7 Ekholm E, Salmi MM, Erkkola R. Eclampsia in Finland in 1990–1994. *Acta Obstet Gynecol Scand* 1999;78:877–82.
- 8 Andersgaard AB, Herbst A, Johansen M, Ivarsson A, Ingemarsson I, Langhoff-Roos J, et al. Eclampsia in Scandinavia: incidence, substandard care, and potentially preventable cases. *Acta Obstet Gynecol Scand* 2006;85:929–36.
- 9 Schutte JM, de Boer K, Briët JW, Pel M, Santema JG, Schuitemaker NW, et al. Maternal mortality in the Netherlands: the tip of the iceberg. *Ned Tijdschr Obstet Gynecol* 2005;118:89–91.
- 10 Zwart JJ, Richters JM, Öry F, de Vries JJ, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371, 000 pregnancies. *BJOG* 2008;115:842–50.
- 11 NVOG. Guideline Hypertensive disease in pregnancy 2004. Available at: <http://nvog-documenten.nl/index.php>. Retrieved July 1, 2008.
- 12 Statistics Netherlands (CBS). Statline, Central Bureau of Statistics. Available at: [http://statline.cbs.nl/StatWeb/publication/?DM\\_SLEN&PA\\_37259ENG&D1\\_1&D2\\_0&D3\\_0&D4\\_44-46&LA\\_EN&HDR\\_T,G2&STB\\_G1,G3&VW\\_T](http://statline.cbs.nl/StatWeb/publication/?DM_SLEN&PA_37259ENG&D1_1&D2_0&D3_0&D4_44-46&LA_EN&HDR_T,G2&STB_G1,G3&VW_T). Retrieved October 2, 2007.
- 13 The Netherlands Perinatal Registry. Perinatal care in the Netherlands 2005. Bilthoven (the Netherlands): The Netherlands Perinatal Registry; 2007.
- 14 Kremer J. Nationwide IVF results 2005 [in Dutch]. Available at: <http://www.nvog.nl/files/landelijkeivfcijfers2005.pdf>. Retrieved October 23, 2007.
- 15 Geirsson RT, Arngrimsson R, Apalset E, Einarsson A, Snaedal G. Falling population incidence of eclampsia. A case– control study of short term outcome. *Acta Obstet Gynecol Scand* 1994;73:465–7.
- 16 Moller B, Lindmark G. Eclampsia in Sweden, 1976–1980. *Acta Obstet Gynecol Scand* 1986;65:307–14.
- 17 Kullberg G, Lindeberg S, Hanson U. Eclampsia in Sweden. *Hypertens Pregnancy* 2002;21:13–21.
- 18 Douglas KA, Redman CW. Eclampsia in the United Kingdom. *BMJ* 1994;309:1395–400.
- 19 Wen SW, Huang L, Liston R, Heaman M, Baskett T, Rusen ID, et al. Severe maternal morbidity in Canada, 1991–2001. *CMAJ* 2005;173:759–64.
- 20 Saftlas AF, Olson DR, Franks AL, Atrash HK, Pokras R. Epidemiology of preeclampsia and eclampsia in the United States, 1979–1986. *Am J Obstet Gynecol* 1990;163:460–5.
- 21 Zhang J, Meikle S, Trumble A. Severe maternal morbidity associated with hypertensive disorders in pregnancy in the United States. *Hypertens Pregnancy* 2003;22:203–12.

- 22 Brace V, Penney G, Hall M. Quantifying severe maternal morbidity: a Scottish population study. *BJOG* 2004;111: 481–4.
- 23 Office for National Statistics. Available at: [http://www.statistics.gov.uk/cci/nugget.asp?id\\_455](http://www.statistics.gov.uk/cci/nugget.asp?id_455). Retrieved November 27, 2007.
- 24 Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: a paradigm shift focusing on systolic blood pressure. *Obstet Gynecol* 2005;105:246–54.
- 25 Royal College of Obstetricians and Gynaecologists. Guideline No. 10(A). The management of severe pre-eclampsia/eclampsia. March 2006. Available at: [www.rcog.org.uk/resources/Public/pdf/management\\_pre\\_eclampsia\\_mar06.pdf](http://www.rcog.org.uk/resources/Public/pdf/management_pre_eclampsia_mar06.pdf). Retrieved November 27, 2007.
- 26 Abi-Said D, Annegers JF, Combs-Cantrell D, Frankowski RF, Willmore LJ. Case-control study of the risk factors for eclampsia. *Am J Epidemiol* 1995;142:437–41.

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